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MAY 03 2007

Appl. No.: 10/722,156  
Atty. Dkt. No.: 10030511-1

**REMARKS**

In view of the following remarks, the Examiner is requested to allow Claims 1-9 and 33-38, the only claims pending and under examination in this application.

***Claim Rejections - 35 USC § 112***

Applicant's acknowledge the withdrawal of the rejection of claims 1-9 under 35 USC § 112, first paragraph.

***Claim Rejections - 35 USC § 102(e)***

The Examiner has rejected claims 1-7 and 9 under 35 USC § 102(e) as being anticipated by Cronin et al. (U.S. Patent No. 6,027,880, issued February 22, 2000, filed October 10, 1995, priority October 26, 1993).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants submit that Cronin et al. fail to disclose each and every element as set forth in claim 1. Specifically, Cronin et al. fail to disclose a method of synthesis wherein degenerate biopolymers are formed at particular feature locations by providing a mixture of biopolymer subunit precursors at particular feature locations.

In the Office Action dated 03/07/2007, the Examiner stated that "In the instant situation, the term 'mixture of biopolymer subunit precursors' is dependent on the previous limitation imposed by the phrase, 'in each round of multiple rounds of subunit additions, providing one or more biopolymer subunit precursors at each of multiple feature locations on said surface.'" The Examiner indicated further that, based on the above, the entire breadth and scope of the claims involve a method which employ a single biopolymer subunit precursor at each of multiple feature locations of the surface. The Examiner concluded that the photolithographic method employed by Cronin et al. would clearly meet this limitation.

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Applicants respectfully disagree with the Examiner's interpretation of the language of claim 1. Applicants submit that the language "providing one or more biopolymer subunit precursors at each of multiple feature locations on said surface to form said plurality of said biopolymers" is a statement describing the general process by which the "plurality" of biopolymers is formed. This statement is subsequently limited by the language "wherein, for one or more feature locations comprising said degenerate biopolymers, said biopolymer subunit precursors comprise a mixture of biopolymer subunit precursors for forming said degenerate biopolymers at said feature location."

The USPTO's standard for claim interpretation is described in *Phillips v. AWH Corp.*, 415 F.3d 1303 (2005), i.e., that during patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. It is clear from claim 1 that the plurality of biopolymers comprising nucleotides at predetermined feature locations on a surface of a substrate includes one or more feature locations comprising degenerate biopolymers. It is equally clear that a mixture of biopolymer subunit precursors is employed to form the feature locations comprising the degenerate biopolymers. Applicants submit that this is the broadest reasonable interpretation of the claim based on the plain language of the claim and the disclosure provided in the specification. Based on a reading of claim 1 and the remaining disclosure of the specification, it would not be reasonable to read these limitations out of claim 1.

Since claim 1 as properly interpreted includes a limitation not taught by Cronin et al., i.e., "wherein, for one or more feature locations comprising said degenerate biopolymers, said biopolymer subunit precursors comprise a mixture of biopolymer subunit precursors for forming said degenerate biopolymer at said feature location," Cronin et al. cannot anticipate claim 1. As such, applicants respectfully request withdrawal of this rejection.

Claims 2 and 3 each depend from claim 1 and are, therefore, patentable over the Cronin et al. reference by virtue of such dependency since claim 1 is patentable over Cronin as demonstrated above.

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Independent claim 4 is patentable over the Cronin et al. reference for reasons similar to those discussed above with regard to the rejection of claim 1. The reference fails to teach at least the following element of claim 4: a method of synthesis wherein a mixture of biopolymer subunit precursors is provided at a feature location to form a feature location comprising degenerate biopolymers. Claims 5-7 and 9 each depend ultimately from claim 4 and are, therefore, patentable over Cronin by virtue of such dependency since claim 4 is patentable over Cronin as demonstrated above.

Additionally, independent claim 4 is patentable over the Cronin et al. reference because Cronin et al. fail to teach at least the following element of claim 4: "dispensing from a dispensing system said biopolymer subunit precursors to said discrete sites."

As acknowledged by the Examiner, Cronin et al. teach a photolithography method utilizing light activation as a means of preparing the oligonucleotide array of the invention. Cronin et al. disclose the following strategy for light-directed oligonucleotide synthesis. "The surface of a solid support modified with photolabile protecting groups (X) is illuminated through a photolithographic mask, yielding reactive hydroxyl groups in the illuminated regions. A 3'-O-phosphoramidite activated deoxynucleoside (protected at the 5'-hydroxyl with a photolabile group) is then presented to the surface and coupling occurs at sites that were exposed to light. Following capping, and oxidation, the substrate is rinsed and the surface illuminated through a second mask, to expose additional hydroxyl groups for coupling. A second 5'-protected, 3'-O-phosphoramidite activated deoxynucleoside is presented to the surface. The selective photodeprotection and coupling cycles are repeated until the desired set of products is obtained."

The above description discloses that an activated deoxynucleoside is "presented to the surface" generally and coupling occurs at sites that were exposed to light. There is no disclosure of dispensing biopolymer subunit precursors from a dispensing system to "discrete sites" as required by claim 4. Claims 5-7 and 9 each

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depend ultimately from claim 4 and are, therefore, patentable over Cronin by virtue of such dependency since claim 4 is patentable over Cronin as discussed.

In light of the remarks presented above, applicants respectfully request withdrawal of the rejection under 35 USC § 102(e) of claims 1-7 and 9.

***Claim Rejections - 35 USC § 103(a)***

The Examiner has rejected claim 8 under 35 USC § 103(a) as being obvious over Cronin et al. (U.S. Patent No.6,027,880) in view of Baldeschwieler et al. (WO 95/25116, published September 21, 1995). The Examiner acknowledges that Cronin et al. do not explicitly disclose that the method of synthesizing the array involve a dispenser comprising at least one droplet dispensing device. However, the Examiner stated that Baldeschwieler et al. disclose a method of synthesizing an array via use of an inkjet technology, wherein the method involves the attachment of molecules onto a substrate surface, for sequential synthesis of polynucleotides wherein the reagents are dispensed from a microdrop dispensing device. According to the Examiner, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Cronin et al. with the teachings of Baldeschwieler et al. to arrive at the claimed invention.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. In re Fine, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. In re Merck & Co., Inc., 231 USPQ 375 (Fed. Cir. 1986). Finally, the prior art reference, or references when combined, must teach or suggest all the claim limitations. In re Royka, 180 USPQ 580 (CCPA 1974). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991).

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Claim 8 depends from claim 4 and therefore includes all the limitations of claim 4. As discussed previously, Cronin et al. fails to teach or suggest at least the following element of claim 4: a method of synthesis wherein a mixture of biopolymer subunit precursors is provided at a feature location to form a feature location comprising degenerate biopolymers. Since the Baldeschwieler et al. reference is relied upon solely for its disclosure of a method of synthesizing an array via use of inkjet technology, and not for any disclosure related to mixtures of biopolymer subunit precursors, it fails to make up for the deficiencies in the Cronin et al. reference.

As such, Applicants submit that the references when combined fail to teach or suggest all the limitations of claim 8. For this reason, Applicants submit that a *prima facie* case of obviousness has not been established and respectfully request withdrawal of the rejection.

The Examiner has rejected claims 1-9 and 33-38 under 35 USC § 103(a) as being obvious over Hanks et al. (Methods in Enzymology, 1991, vol. 200, pages 525-532) in view of Baldeschwieler et al. The Examiner stated that Hanks et al. disclose a method of using degenerate oligonucleotide probes so as to identify clones that encode protein kinases. According to the Examiner it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fabricate a microarray comprising a plurality of degenerate oligonucleotide probes for the well known benefit of simultaneously identifying a plurality of homologous genes of interest.

As discussed previously, each of claims 1-9 have as an element a method of synthesis wherein a mixture of biopolymer subunit precursors is provided at a feature location to form a feature location comprising degenerate biopolymers.

While the Examiner suggests that Hanks et al. explicitly disclose that degenerate oligonucleotide probes are employed in a hybridization assay, the Examiner has not specified that Hanks et al. disclose a method of synthesis wherein a mixture of biopolymer subunit precursors is provided at a feature location to form a

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feature location comprising degenerate biopolymers. Since the Baldeschwieler et al. reference is relied upon solely for its disclose of a method of synthesizing an array via use of inkjet technology, and not for any disclosure related to mixtures of biopolymer subunit precursors, it fails to make up for the deficiencies in the Hanks et al. reference. As such, the references fail to teach or suggest all of the claim limitations. For this reason, Applicants respectfully request withdrawal of the rejection.

Claim 33 recites the element of "dispensing from a dispensing system said biopolymer subunit precursors to said discrete sites wherein, for one or more of said feature locations comprising said degenerate biopolymers, a mixture comprising a predetermined ratio of said biopolymer subunit precursors for forming said degenerate biopolymers is dispensed in a droplet manner at each of said feature locations comprising said degenerate biopolymers."

The argument presented in response to the rejection of claims 1-9 above applies a *fortiori* to the rejection of claim 33. As discussed above, the Examiner has not specified that Hanks et al. disclose a method of synthesis wherein a mixture of biopolymer subunit precursors is provided at a feature location to form a feature location comprising degenerate biopolymers, much less a mixture comprising a predetermined ratio of said biopolymer subunit precursors for forming said degenerate biopolymers. As the Baldeschwieler et al. reference is relied upon solely for its disclose of a method of synthesizing an array via use of inkjet technology, and not for any disclosure related to mixtures of biopolymer subunit precursors, it fails to make up for the further deficiencies in the Hanks et al. reference.

Claims 34-38 each depend from claim 33 and are, therefore, patentable over Hanks et al. in view of Baldeswieler et al. by virtue of such dependency since claim 33 is patentable over the references as discussed.

As part of the rejection of claims 1-9 and 33-38 under 35 USC § 103(a), the Examiner stated that Applicants' definition of the term "mixture" does not exclude a

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plurality of same nucleotides, and that the instant claims encompass such an embodiment.

Applicants submit that, based on the plain meaning of the term "mixture", one of ordinary skill in the art would understand the term to mean at least two different biopolymer subunit precursors in this context. By way of example, Applicants direct the Examiner's attention to the following definitions of the term mixture:

- a) "a portion of matter consisting of two or more components in varying proportions that retain their own properties" (Merriam Webster Online Dictionary, [www.merriamwebster.com](http://www.merriamwebster.com))
- b) "a combination of several different kinds" (Merriam Webster Online Dictionary, [www.merriamwebster.com](http://www.merriamwebster.com))
- c) "The word *mixture* is used to describe a gaseous or liquid or solid phase containing more than one substance, when the substances are all treated in the same way . . ." (CRC Handbook of Chemistry and Physics, CRC Press, Inc. (1983)).

Based on these definitions, and the general understanding of one of ordinary skill in the art, Applicants submit that the term "mixture" does exclude a plurality of same nucleotides. The Examiner has not indicated that either Hanks et al. or Baldeswieler et al. teach or suggest a "mixture" of biopolymer subunit precursors as so defined. As such, the Examiner has not shown that the prior art reference, or references when combined, teach or suggest all the claim limitations.

Applicants submit that based on the above a prima facie case of obviousness has not been established. For this reason, Applicants respectfully request withdrawal of the rejection.

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**CONCLUSION**

In view of the remarks above, the Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. AGILENT 50-1078, order number 10030511-1.

Respectfully submitted,

Date: May 3, 2007

By: 

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